POOR LEGIBILITY

ONE OR MORE PAGES IN THIS DOCUMENT ARE DIFFICULT TO READ
DUE TO THE QUALITY OF THE ORIGINAL

Acta Medica Scandinavica. Vol. 174, fasc. 2, 1963

From the Medical Department (Head: Rolf Jorde, M. D.),
Hordaland County Hospital, Stord, Norway

Fatal Aplastic Anaemia Following Use of Potassium Perchlorate in Thyrotoxicosis

By

Nils Gjemdal

Antithyroid drugs are often used in the treatment of thyrotoxicosis. Several types of drugs are available, but they may all give rise to undesirable reactions.

Crooks and Wayne (2) in 1960 made a comparison of potassium perchlorate, methylthiouracil and carbimazole in the treatment of thyrotoxicosis in over 450 patients. The incidence of untoward reactions from potassium perchlorate was comparatively low. Untoward reactions were more common with high dosage (1,500—2,000 mg daily) than with low dosage (600—1,000 mg daily). The authors considered potassium perchlorate the drug of choice.

Johnson and Moore (6) reviewed 818 published cases of thyrotoxicosis treated with potassium perchlorate and found 36 cases (4 %) presenting toxic reactions including exanthema, gastro-intestinal disturbances, pyrexia, sore throat, lymphadenopathy and neutropenia. They themselves reported a case of aplastic anaemia.

Hoping to reduce the incidence of toxic reactions from antithyroid therapy Blorstad and Vogt (1) tried a combined treatment with potassium perchlorate and propylthiouracil, using comparatively small amounts of each substance. By the use of 400 mg potassium perchlorate and 400 mg propylthiouracil daily as initial dosage, Vogt (8) reported few untoward effects and satisfactory results in most cases.

Hernberg (4) states that experiences with the use of potassium perchlorate are not exclusively good, but considers the substance a useful alternative in patients who are hypersensitive to other antithyroid compounds.

Four cases of aplastic anaemia due to potassium perchlorate, all of them fatal, have so far appeared in the literature. These patients all received moderate doses, viz., 1,000 mg (6), 800 mg (5, 7) and 600 mg (3) daily.

In an editorial in Brit. med. J. (10) dealing with potassium perchlorate and aplastic anaemia it was pointed out that aplastic anaemia is probably more apt to occur following the use of potassium perchlorate than the organic antithyroid drugs more commonly used during recent years.

Submitted for publication January 16, 1963.

Case report

A woman, aged 82, was admitted to hospital on Sept. 9, 1961 because of malaise, weakness, dyspepsia, loss of appetite and weight, palpitations and loss of hair. A diagnosis of thyrotoxicosis was made. Amongst the laboratory findings should be mentioned a white blood count 3,700/mm³, platelet count 225,000/mm³, Hb 94 % and ESR 8 mm/hr.

Treatment with Tapazole® in a dosage of 20 mg daily was started. About three weeks later the patient became subfebrile, with pain, swelling, redness and restricted movements of the right wrist. Platelets dropped to 154,000/mm³. Tapazole® was withdrawn and treatment with methylthiouracil in a dosage of 300 mg daily was started. Under this treatment marked improvement was noted and the patient was discharged with 200 mg of methylthiouracil daily. During the subsequent months the dosage was reduced to 100 mg daily and later to 100 mg every second day.

The patient was re-admitted on April 7, 1962 because of bronchopneumonia. The white cell count was 3,300/mm³, platelet count 225,000/mm³. The patient received Proca-penicillin. A rash developed, but disappeared following withdrawal of methylthiouracil and Proca-penicillin. Later, pyuria developed and was treated with a sulphonamide preparation. Again, a rash developed, but disappeared following withdrawal of sulphonamide. Treatment with potassium perchlorate in a dosage of 600 mg daily was then started. Blood values remained normal until July 18, 1962, when the white cell count dropped to 2,600/mm³. Platelets were not counted, but were scanty in a blood smear. The haemoglobin content was 84 %. The dosage of potassium perchlorate was reduced to 400 mg daily.

The patient was admitted again on Aug. 15, 1962 because of bleeding manifestations, viz., epistaxis, numerous petecchiae and ecchymoses. Slight sacral and crural oedema was noted. Potassium perchlorate was withdrawn. The urine was normal. The haemoglobin content was 40 % and the red cell count 2,100,000/mm³. The white cell count was 2,100/mm³, with 1 % basophils, 2 % monocytes, 5 % segmented forms and 92 % lymphocytes. Slight anisocytosis and poikilocytosis were noted. The platelet count 32,000/mm³, ESR 77 mm/hr, PP 80 %. sternal smear showed very few cells, most them red blood cells, a few mononuclears and few platelets. Megacaryocytes were not seen.

The white cell count ranged between 2,500 and 1,300/mm³. For a while the platelet count remained at 39,000/mm³, but then dropped to 19,000/mm³. Otherwise the blood values remained unchanged apart from a transient rise in the percentage of segmented white cells with a corresponding fall in the percentage of lymphocytes, but normal levels were never noted.

The patient was treated with prednisone, and a transient reduction of the bleeding manifestations was noted. She also received blood transfusions, courses of Achromycin® and injections of a testosterone preparation, Sustanon®, 500 mg weekly. Her condition deteriorated and she died on Oct. 20, 1962.

Discussion

The criteria for establishing a diagnosis of aplastic anaemia (9) include anaemia, marked granulocytopenia, marked thrombocytopenia and hypocellular bone marrow. They were all present in the case reported above.

A rash developed following the administration of sulphonamides, likewise during treatment with methylthiouracil. In the latter event, however, the reaction might be due to the concurrent administration of Proca-penicillin. Under treatment with Tapazole, arthritis and a fall in the platelet count were noted. In this patient several drugs seemed to cause untoward reactions. As to her aplastic anaemia, however, causes other than potassium perchlorate could not be found. The initial signs of blood dyscrasia should probably have warranted stricter precautions than merely a reduction of the potassium perchlorate dosage.

Krevans et al. (7) used potassium perchlorate for some time in the treatment of thyrotoxicosis. They found the drug useful in a large proportion of cases, especially in those patients having previously shown sensitivity to propylthiouracil or methimazole or both drugs. These authors, however, later observed an instance of fatal aplastic anaemia secondary to the use of potassium perchlorate. As this seems irreversible, the authors later warned against further use of this drug in therapy except under unusual circumstances.

Potassium perchlorate carries a considerable risk, as indicated by the fact that the four published cases of aplastic anaemia following its use all ended fatally. The daily dose in the case reported above was 600 mg, which is considered very moderate.

If potassium perchlorate is to be used for treatment of thyrotoxicosis, it should probably not at any rate be given to patients who have shown untoward reactions to any other drug.

Summary

A case of fatal aplastic anaemia due to treatment of thyrotoxicosis with potassium perchlorate is reported. The highest dosage level was 600 mg daily. The literature dealing with potassium perchlorate and its complications is briefly reviewed. The patient in question had previously showed untoward reactions to other drugs, and it is probably advisable to avoid the use of potassium perchlorate in patients with previous signs of drug idiosyncrasy.

References

1. Blørstad, Ø. & Vogt, J. H.: Combined treatment of thyrotoxicosis with perchlorate and propylthiouracil. Acta med. scand. *171:* 283, 1962.
2. Crooks, J. & Wayne, E. J.: A comparison of potassium perchlorate, methylthiouracil, and carbimazole in the treatment of thyrotoxicosis. Lancet *I:* 401, 1960.
3. Fawcett, J. W. & Clarke, C. W. F.: Aplastic anaemia due to potassium perchlorate. Brit. med. J. *I:* 1537, 1961.
4. Hernberg, C. A.: Behandling av thyreotoxikos och thyreohypofysärt syndrom. Nord. Med. *I:* 820, 1957.
5. Hobson, Q. J. G.: Aplastic anaemia due to treatment with potassium perchlorate. Brit. med. J. *I:* 1368, 1961.
6. Johnson, R. S. & Moore, W. G.: Fatal aplastic anaemia after treatment of thyrotoxicosis with potassium perchlorate. Brit. med. J. *I:* 1369, 1961.
7. Krevans, J. R., Asper, S. P. & Rienhoff, W. F.: Fatal aplastic anaemia following use of potassium perchlorate in thyrotoxicosis. J. Amer. med. Ass. *II:* 162, 1962.
8. Vogt, J. H.: Personal communication 1962.
9. Wintrobe, M. M.: Clinical hematology. 4th edit. Lea & Febiger, Philadelphia 1958.
10. Editoral: Potassium perchlorate and aplastic anaemia. Brit. med. J. *I:* 1520, 1961.